Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

PET imaging in head and neck cancer.

Bibliographic Source(s)

Yoo J, Walker-Dilks C, Henderson S. PET imaging in head and neck cancer. Toronto (ON): Cancer Care Ontario (CCO); 2012 Feb 9. Various p. (PET Recommendation Report; no. 2). [97 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Yoo J, Walker-Dilks C. PET imaging in head and neck cancer: recommendations. Toronto (ON): Cancer Care Ontario (CCO); 2009 Jan 19. 43 p. (Recommendation report - PET; no. 2).

The PET RECOMMENDATION report, initially the full original Guideline, over time will expand to contain new information emerging from reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

Recommendations

Major Recommendations

Diagnosis/Staging

- Positron emission tomography (PET) is recommended in the M and bilateral nodal staging of all patients with head and neck squamous cell carcinoma where conventional imaging is equivocal, or where treatment may be significantly modified.
- PET is recommended in all patients after conventional imaging and in addition to, or prior to, diagnostic panendoscopy where the primary site is unknown.
- PET is recommended for staging and assessment of recurrence of patients with nasopharyngeal carcinoma if conventional imaging is equivocal.

Recurrence/Restaging

PET is recommended for restaging patients who are being considered for major salvage treatment, including neck dissection.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Head and neck cancer

Guideline Category

Diagnosis

Evaluation

Management

Technology Assessment

Clinical Specialty

Nuclear Medicine

Oncology

Otolaryngology

Radiation Oncology

Radiology

Surgery

Intended Users

Physicians

Guideline Objective(s)

- To evaluate:
  - What benefit to clinical management positron emission tomography (PET) or positron emission tomography/computed tomography (PET/CT) contributes to the diagnosis or staging of head and neck cancer?
  - What benefit to clinical management PET or PET/CT contributes to the assessment of treatment response for head and neck cancer?
  - What benefit to clinical management PET or PET/CT contributes when recurrence of head and neck cancer is suspected but not proven?
  - What benefit to clinical management PET or PET/CT contributes to restaging at the time of documented recurrence for head and neck cancer?
  - What is the role of PET when a solitary metastasis is identified at the time of recurrence and the metastasectomy is being contemplated?
- To guide the Ontario PET Steering Committee in their decision making concerning indications for the use of PET imaging
- To inform clinical decision making regarding the appropriate role of PET imaging and in guiding priorities for future PET imaging research

Target Population

Patients with head and neck cancer

Interventions and Practices Considered

1. Positron emission tomography (PET)
2. Positron emission tomography/computed tomography (PET/CT)

Major Outcomes Considered

Sensitivity and specificity of positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search

A scoping review undertaken by the Program in Evidence-based Care (PEBC) methodologist to identify any existing systematic reviews on positron emission tomography (PET) imaging in the cancers of interest yielded such a review. The U.K. Health Technology Assessment (HTA) systematic review (referred to as the HTA review from this point forward) evaluated the effectiveness of fluorodeoxyglucose (FDG) imaging in several selected cancers, including head and neck. The document included systematic reviews and individual primary studies dating from 2000 to August 2005. Because the HTA review sufficiently covered the questions and methodologies of interest to this recommendation report, its results were used for the evidence base from 2000 to August 2005, and its search strategies were performed in MEDLINE and EMBASE to update the literature to July 2011. The update strategies for MEDLINE and EMBASE are in Appendices 1 and 2 in the original guideline document, respectively.

Study Selection Criteria

All systematic reviews and primary studies in the HTA review that addressed the questions of interest in this recommendation report (diagnosis, staging, treatment response, recurrence, and restaging) were included. The inclusion criteria of the HTA review were employed to select systematic reviews and primary studies identified in the update search.

The inclusion criteria for systematic reviews included in the HTA review and used in the update were:

- Dedicated to FDG PET in the selected cancers in humans
- Contained evidence related to diagnostic accuracy, change in patient management, clinical outcomes, or treatment response

The inclusion criteria for primary studies included in the HTA review and used in the update were:

- Prospective clinical study of dedicated FDG PET in a single cancer of interest
- Study published after the search date of a robust systematic review covering that cancer management decision
- Study published as a full article in a peer-reviewed journal
- Study reported evidence related to diagnostic accuracy, change in patient management, or clinical outcomes
- Study included ≥12 patients with the cancer of interest
- Study used a suitable reference standard (pathological confirmation and clinical follow-up) when appropriate

The citations and abstracts from the update searches were reviewed by the PEBC research coordinator and marked as relevant or not relevant, according to the inclusion criteria from the HTA review, and were classified by disease site. The research coordinator and the clinical lead for each

Disease Site Group reviewed the relevant citations and full text of the articles for final decision on inclusion.

Number of Source Documents

The Health Technology Assessment (HTA) review results for head and neck cancer included five systematic reviews and 31 primary studies. The 2005 to 2008 update included two systematic reviews and 35 primary studies. The 2008 to 2011 update included 18 primary studies and two systematic reviews.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Synthesizing the Evidence

The Health Technology Assessment (HTA) review did not pool individual studies. Data were extracted into separate tables for systematic reviews and primary studies for each type of management decision. The same approach was used for data extraction for the evidence from August 2005 to June 2008 and subsequently from July 2008 to July 2011. Full text and data extractions of the studies from the update search were provided to the clinical lead author to aid in the formulation of the recommendations. Telephone conferences and email correspondence between the clinical lead and the Program in Evidence-Based Care (PEBC) methodologist took place to clarify details and answer questions.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Disease Site Group (DSG) Consensus Process

The clinical lead author wrote summaries of the key evidence, draft recommendations, and qualifying statements for the questions pertaining to diagnosis/staging, assessment of treatment response, and recurrence/restaging. The ensuing documents were circulated to all members of the gastrointestinal (GI) DSG and discussed during a teleconference. The recommendations that were generated during this process are referred to below as the DRAFT DSG Recommendations. The intent of these recommendations was to guide discussion at the consensus meeting. This step was not considered necessary for the 2011 update because evidence was consistent with the existing evidence base and no global changes were made to the existing recommendations.

Provincial Consensus Process

The consensus meeting on 19 September 2008 was conducted as follows:

- Consensus meeting participants sat at tables specifically set up to discuss a particular disease site (colorectal, esophageal, head and neck,

and melanoma). The Head and Neck table held the clinical lead and any other Head and Neck DSG members attending, in addition to other invited health professionals.
- The recommendations and summary of key evidence drafted by the clinical lead and refined and confirmed by the Head and Neck DSG were presented by the clinical lead to the group at the Head and Neck table.
- During small-group discussion at the Head and Neck table in the morning and discussion among the entire consensus meeting participants in the afternoon, the recommendations underwent further refinement and modification. The attendees voted on the revised recommendations to indicate their extent of agreement on a scale from 1 to 9 (1 indicating strong agreement, 5 indicating no agreement or disagreement, and 9 indicating strong disagreement).

After the consensus meeting, the exact wording of the recommendations was slightly modified for consistency with the recommendations resulting from the other disease discussions. These modifications included using emphatic, unambiguous language (i.e., *positron emission tomography [PET] is recommended*...) and removing the need to distinguish between PET and positron emission tomography/computed tomography [PET/CT]. It was made clear at the consensus meetings that PET imaging alone is being phased out and PET/CT imaging is the current standard. Thus, the term PET is used to cover PET and PET/CT imaging. These recommendations are referred to as the FINAL RECOMMENDATIONS and were the foundation for any new or updated recommendations identified in the literature updates. Any updates to the recommendations arising from subsequent literature updates precede the original recommendation.

The committee has not been reconvened for the 2011 update because the evidence base is consistent with the existing recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

These recommendations are based on an evidentiary foundation consisting of one recent high-quality U.K. Health Technology Assessment systematic review that included systematic review and primary study literature for the period from 2000 to August 2005, an update of that systematic review undertaken to retrieve the same level of evidence for the period from August 2005 to June 2008, and a subsequent literature search conducted to retrieve literature from June 2008 to July 2011. The 2005 to 2008 update included two systematic reviews and 35 primary studies. The 2008 to 2011 update included 18 primary studies and two systematic reviews.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Diagnosis/Staging

- One systematic review of four primary studies and one additional primary study showed positron emission tomography (PET) was sensitive and specific and useful where doubt exists (computed tomography/magnetic resonance imaging [CT/MRI] gave different and less optimal results). PET changed stage and treatment planning. In the 2008-2011 update, studies reviewed all identified that PET was superior to conventional imaging for the detection and staging of head and neck squamous cell carcinoma. Additionally, several studies indicated that the addition of PET improved primary tumour delineation and nodal staging and subsequently changed the clinical management of several patients in each study.
- Two systematic reviews (each with eight primary studies) and two additional primary studies showed that PET can detect primary unknown tumours in patients with cervical lymph node metastases. PET detects 30% of primary tumours, including those missed by conventional imaging. In the 2005-2008 update, one primary study showed that PET is better than conventional imaging in detecting site of primary tumour. In the 2008-2011 update, one primary study indicated that patients with cervical metastasis and an unknown primary site after undergoing conventional imaging or clinical examination benefit from PET/CT prior to panendoscopy.
- Seven primary studies showed that PET scanning was more accurate than conventional imaging in identifying metastatic disease. In the 2008-2011 update, one study identified PET as being a valuable staging tool for the detection of nasopharyngeal carcinoma and changed patient management in 16 of 48 patients.

Recurrence/Restaging

Patients being evaluated for locoregional recurrence and considered for salvage should have PET in order to help tailor further therapy. Examples include larynx, skull base and nasopharynx, salivary gland, and neck disease. In the 2008-2011 update, studies confirmed the effectiveness of PET in assessing for recurrence of head and neck squamous cell carcinomas in patients. Contrary to this, another study found PET to be of no additional value to determine the persistence of nodal disease after chemoradiotherapy. Additionally, a different study supports the use of PET-directed management of the neck after chemoradiotherapy in that it spares unnecessary neck dissections.

Potential Harms

False positive and false negative results

Qualifying Statements

Qualifying Statements

Diagnosis/Staging

- This report makes no distinction between studies examining (PET) and those examining positron emission tomography/computed tomography (PET/CT).
- Conventional imaging refers to CT and/or magnetic resonance imaging (MRI) unless otherwise specified.
- Retrospective design studies were excluded from this review, but several exist favouring the use of PET for head and neck cancer.
- With respect to primary site (T):
  - PET appears to be more accurate for the diagnosis of primary tumours, especially in cases where CT/MRI results are equivocal.
  - PET can identify the primary site in 30% of cases when undetected by clinical assessment and conventional imaging.
  - PET can detect some synchronous primaries that may be missed by other modalities.
- With respect to regional nodes (N):
  - In the clinically N-0 neck, PET does not appear to be better than conventional imaging, because of an unacceptably high false-negative rate. There is little evidence that PET leads to change in patient management.
- There was moderate evidence that PET scanning changed nodal staging status and/or radiation treatment planning. However, in many cases there was no pathologic confirmation of PET versus conventional imaging discrepancy. Exceptions were cases where distant metastatic disease was identified by PET and changed treatment.
- With respect to distant disease (M):
  - There is strong evidence that PET imaging is valuable in detecting distant metastatic disease and is better than conventional imaging. The advantage of PET is overwhelming for patients at high risk for distant disease, which includes locally advanced disease and nasopharyngeal carcinoma. The substantial incidence of false-positive rates of PET may mitigate the advantages for low-risk patients.

Recurrence/Restaging

- With respect to recurrence and tumour surveillance after treatment, the evidence suggests that sites of disease that are clinically accessible for assessment did not benefit from PET imaging. However, for disease sites that were either not clinically accessible or difficult to examine, PET imaging showed significant advantages over conventional evaluation.
    - Larynx: moderate evidence that PET is beneficial/better than conventional imaging in detecting recurrent disease. PET also reduced the need for debilitating laryngeal biopsies.
    - Skull base and nasopharynx: moderate evidence that PET is beneficial/better than conventional imaging in detecting recurrent disease
    - Salivary gland: moderate evidence suggesting an advantage with PET
    - Nodal disease: For N+ patients, moderate evidence exists that PET is better than conventional imaging in detecting the status of residual disease following radiotherapy or chemoradiotherapy. The use of PET reduced both false-positive and false-negative rates compared to the gold standard. It is of relevance to note that clinical trials are currently being conducted in Ontario on this matter. Once published, they will be evaluated for inclusion and incorporated into the recommendation report in subsequent updates.
    - There is evidence that PET detects distant relapse. There is strong evidence that the detection of distant disease leads to major changes in patient management in the salvage setting.
- With respect to the role of PET in assessing status of neck lymphadenopathy following radiation or chemoradiation, moderate evidence suggests that PET-directed management of the neck after therapy, appropriately spares neck dissections in patients with PET-negative residual CT abnormalities

Disclaimer

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Yoo J, Walker-Dilks C, Henderson S. PET imaging in head and neck cancer. Toronto (ON): Cancer Care Ontario (CCO); 2012 Feb 9. Various p. (PET Recommendation Report; no. 2). [97 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2009 Jan 19 (revised 2012 Feb 9)

Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

Guideline Developer Comment

The Program in Evidence-Based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

Source(s) of Funding

The Program in Evidence-based Care (PEBC) is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Guideline Committee

Head and Neck Disease Site Group

Composition of Group That Authored the Guideline

For a current list of past and present members, please see the Cancer Care Ontario Web site .

Financial Disclosures/Conflicts of Interest

Not stated

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Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

Availability of Companion Documents

The following are available:

- PET imaging in head and neck. Summary. Toronto (ON): Cancer Care Ontario; 2012 Feb 9. 8 p. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario (CCO) Web site.
- Program in Evidence-Based Care (PEBC) handbook. Toronto (ON): Cancer Care Ontario (CCO); 2012. 14 p. Electronic copies: Available in PDF from the CCO Web site.

Patient Resources

None available

NGC Status

This summary was completed by ECRI Institute on April 26, 2010. This NGC summary was updated by ECRI Institute on September 6, 2013.

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